3. Barza M, Ioannidis JP, Cappelleri JC, Lau J. Single or multiple daily doses of aminoglycosides: a meta-analysis. BMJ **1996**; 312:338–45.
4. Leibovici L, Paul M, Poznanski O, et al. Monotherapy versus beta-lactam–aminoglycoside combination treatment for Gram-negative bacteremia: a prospective, observational study. Antimicrob Agents Chemother **1997**; 41:1127–33.
5. Falagas ME. Monotherapy versus beta-lactam–aminoglycoside combination therapy for gram-negative bacteremia. Antimicrob Agents Chemother **1997**; 41:2593–4.
6. Safdar N, Handelsman J, Maki DG. Does combination antimicrobial therapy reduce mortality in gram-negative bacteraemia: a meta-analysis. Lancet Infect Dis **2004**; 4:519–27.

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Failure of Primaquine Therapy for the Treatment of *Plasmodium ovale* Malaria

Sir—The high relapse rate of patients with *Plasmodium vivax* malaria has been highlighted in a review article by Baird et al. [1]. Widespread resistance to the standard regimen of primaquine (15 mg daily for 14 days) was proposed as the most likely cause [1]. A regimen of 0.5 mg/kg primaquine daily for 14 days (total dose, 7 mg/kg) was recommended "on the basis of superior efficacy and good tolerability and safety in nonpregnant patients without glucose-6-phosphate dehydrogenase deficiency" [1, p. 1336]. To our knowledge, only 2 reports of failure of primaquine treatment for *P. ovale* malaria have been published in the English-language literature [2, 3], but compliance with therapy in these reports was unclear. We report another 3 cases of *P. ovale* malaria relapse after standard treatment with primaquine.

Patient 1 was a 17-year-old Belgian boy who was referred in 2002, six weeks after he returned from a 1-month stay in Ghana. He had received adequate mefloquine prophylaxis. He was suspected to have malaria and had been given quinine (1.5 g daily for 5 days) and doxycycline (100 mg daily for 7 days). *P. ovale* infection was confirmed by the findings on the initial thick blood smear, and a standard regimen of primaquine was administered. Seven weeks later, the patient presented again with fever, and a diagnosis of relapse was made (on the basis of a finding of 50 *P. ovale* trophozoites per μL). He was then treated with chloroquine (1.5 g in a 3-day course) and primaquine (22.5 mg daily for 3 weeks; total dose, 7 mg/kg).

Patient 2 was a 14-year-old Belgian boy who presented in September 2004, on the second day of treatment with atovaquone-proguanil for *P. ovale* malaria, which had been diagnosed at another institution. Parasites were still found by our laboratory (393 trophozoites per μL). In 2001, the patient had traveled for 2 months in Uganda without receiving prophylaxis; he had experienced a first attack of *P. ovale* malaria in February 2002, which was treated with chloroquine only, and a second one in March 2003, which was treated with atovaquone-proguanil and primaquine (45 mg weekly for 6 weeks; total dose, 5 mg/kg). This third episode was considered a relapse that occurred despite standard (although unusual) primaquine therapy [1], and it was treated with chloroquine and primaquine (22.5 mg daily for 3 weeks; total dose, 8 mg/kg).

Patient 3 was a 22-year-old Belgian man who presented with fever in 2004, three months after a 4-month stay in Nigeria. He had received adequate mefloquine prophylaxis. *P. ovale* infection was later identified at the Institute for Tropical Medicine, Antwerp. Treatment with quinine-doxycycline, already initiated, was completed with a standard primaquine regimen. Fever recurred 2 weeks later, and *P. ovale* organisms were found again. The patient was then given chloroquine and primaquine (30 mg daily for 4 weeks; total dose, 10 mg/kg).

Although administration of primaquine therapy was not directly observed, compliance appeared to have been perfect for all 3 patients, after thorough inquiry. None had traveled to areas where *P. ovale* malaria is endemic since their previous attacks. After treatment with high doses of primaquine, no relapses occurred (with 6–36 months of follow-up).

Therapy failure despite standard primaquine regimen is exceptional for *P. ovale* infection, as we have observed in our long experience and as evidenced by the very few reported cases. However, we have documented 3 such cases in the past 3 years. Reinfection was excluded as a possibility, and noncompliance with therapy was extremely unlikely. In conclusion, relapse of *P. ovale* malaria despite treatment with a standard primaquine regimen does occur, and clinicians should be aware that resistance may be present in *P. ovale,* as it has emerged in *P. vivax* [1, 4]. Our findings also give support to the recent recommendation of the Centers for Disease Control and Prevention to eradicate *P. ovale* hypnozoites with a regimen for adults of 30 mg primaqine base (0.5 mg/kg) by mouth daily for 14 days [5].

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References

1. Baird JK, Hoffman SL. Primaquine therapy for malaria. Clin Infect Dis **2004**; 39:1336–45.
2. Nathwani D, Currie PF, Smith CC, Khaund R. Recurrent *Plasmodium ovale* infection from Papua New Guinea—chloroquine resistance or inadequate primaquine therapy? J Infect **1991**; 23:343–4.
3. Rombo L, Edwards G, Ward SA, et al. Seven patients with relapses of *Plasmodium vivax* or *P. ovale* despite primaquine treatment. Trop Med Parasitol **1987**; 38:49–50.
4. Spudick JM, Garcia LS, Graham DM, Haake DA. Diagnostic and therapeutic pitfalls associated with primaquine-tolerant *Plasmodium vivax.* J Clin Microbiol **2005**; 43:978–81.
5. Centers for Disease Control and Prevention. Treatment for malaria: guidelines for clinicians, part 2—general approach and uncomplicated malaria. Available at: http://www.cdc.gov/malaria/diagnosis_treatment/clinicians2.htm. Accessed 27 July 2005.

Presented in part: Data on patient 1 have been presented at the 8th Conference of the International Society of Travel Medicine, New York, May 2003 (abstract PO 05.09). Data on patients 1 and 2 are mentioned in a paper submitted to another periodical that describes all patients with non-*falciparum* malaria diagnosed in the past 5 years.

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It's My Turn

Sir—I was disappointed with Dr. Tenenbaum's [1] assessment that there is little that the Infectious Diseases Society of America (IDSA) itself can do to discipline or censure a member who appears as an expert witness in judicial proceedings and gives unscientific, prejudicial testimony. His first suggested recourse was to bring the matter to the attention of the relevant state medical board [1]. I think it unlikely that a state board would be interested in dissecting what its members would perhaps see as arcane disagreements over scientific minutiae. The state boards are occupied with cases concerning physicians who have drug, alcohol, or legal problems. I did call the New York State Office of Professional Misconduct, and they are not interested in evaluating scientific disagreements; I would have to prove perjury before presenting a case to them. They suggested that I seek a different venue. The fact that Dr. Tenenbaum offers no information detailing prior successes for this course of action suggests that it is, perhaps, a gratuitous recommendation and one for which he has few actual outcome data.

Dr. Tenenbaum's assertion that the "IDSA currently has neither the administrative staff nor the funds to perform these duties without sacrificing its advocacy and educational responsibilities" [1, p. 1392], I think begs the question. How many malpractice cases in the US each year involve testimony from an infectious diseases expert witness? Of these cases, how many would involve testimony that could be considered unscientific? How much time and effort would it take to locate these cases and take appropriate disciplinary action? A back-of-the-envelope analysis of these numbers would be helpful in our assessment of this decision.

This brings me to my last point. I have always been surprised at the low level of democracy and transparency in our professional societies. I have written to the IDSA in the past regarding unscientific expert testimony, and was told that a statement was being prepared. In the age of the Internet, I would think that minutes from any meeting held by the IDSA could be posted on the society's Web site and reviewed by members; that members could be polled regarding policy decisions; and that there could be financial transparency with regard to income, expenses, and prioritization of funds. As it stands now, a decision has been made in which I have had no input and for which there is no established appeal process. An argument has been posited regarding the financial inability of the IDSA to review expert witness testimony. I have been given no real data and have no way to assess this argument's validity. Why is this particular article exempt from the typical standards of proof and argument? There should be more input from the rank-and-file membership of the IDSA regarding these broad policy decisions and a deeper dialogue between the leadership and membership of the IDSA.

Perjury by an infectious diseases expert who is a member of the IDSA hurts us all and demeans and diminishes our authority as infectious diseases specialists. Attempts to remedy this problem through lobbying have been woefully ineffective. We could, tomorrow, begin to make it very difficult for a physician to continue to give unscientific testimony. I would like to understand the specific constraints, financial and otherwise, that prevent this from happening.

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Philip S. Smith

References

1. Tenenbaum MJ. Expert witness guidelines: it's our turn. Clin Infect Dis 2005; 40:1393–4.

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Reply to Smith

Sir—Even though I am the chair of the Clinical Affairs Committee, I wrote the introduction [1] to the Infectious Diseases Society of America's (IDSA's) expert witness guidelines [2] as a personal statement, not as spokesperson for the IDSA, and I will respond to Dr. Smith's letter [3] in the same capacity.

As I wrote [1], the actual number of infectious diseases physicians named in malpractice cases annually is not known and, since infectious diseases expert witness testimony is often given in actions in which no infectious diseases physician is a defendant, I believe the total number of such annual testimonies is substantial. Also, Dr. Smith uses the example of "unscientific testimony" as one that should obviously be reviewed. However, save for actual perjury, which I believe rarely occurs, no one has defined "unscientific" or "prejudicial" testimony, and I suspect, if someone did, that many expert witness testimonies could be reviewed.

I still strongly feel the IDSA should not be the enforcer of these guidelines, but I never stated nor meant to imply that there were extant nationally established means to punish physicians who give false or biased testimony. I reported that the American Medical Association has made medical expert witness standards one of its legislative priorities and that the association has suggested that disciplinary action be dealt with at the state level [1]. However, until the lawsuit *Fullerton v Florida Medical Association* [4], in which the defendant is being sued by a physician whose expert witness testimony the Florida Medical Association felt fell "below reasonable standards," is settled, I believe other state